```
=> d his

     (FILE 'HOME' ENTERED AT 10:47:48 ON 27 JAN 2005)

     FILE 'CAPLUS' ENTERED AT 10:47:56 ON 27 JAN 2005
L1             2 S WO9626201/PN
               SELECT L1 2 RN
L2         37880 S E1-E51

     FILE 'REGISTRY' ENTERED AT 10:49:06 ON 27 JAN 2005
L3             1 S 182167-02-8/RN
               SET NOTICE 1 DISPLAY
               SET NOTICE LOGIN DISPLAY

     FILE 'CAPLUS' ENTERED AT 10:51:44 ON 27 JAN 2005
L4        124379 S ESTROGEN OR ?ESTRADIOL OR ?ESTRIOL OR MESTRANOL
L5            70 S L3 OR ACOLBIFENE OR EM(W)652 OR  SCH(W)57068
L6            54 S L4(L)L5
L7            24 S L6 NOT PY>=2002

     FILE 'MEDLINE, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 11:02:22 ON 27 JAN
     2005
L8            69 S L7
L9            25 DUP REM L8 (44 DUPLICATES REMOVED)

     FILE 'USPATFULL, USPAT2' ENTERED AT 11:16:22 ON 27 JAN 2005
L10           89 S L6
               E LABRIE F/IN
L11            9 S E4 AND L10
```

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=> s wo9626201/pn
L1             2 WO9626201/PN

=> select l1
ENTER ANSWER NUMBER OR RANGE (1-):2
ENTER DISPLAY CODE (TI) OR ?:rn
E1 THROUGH E51 ASSIGNED

=> s e1-e51
         14732 108-46-3/BI
          3617 110-87-2/BI
          7945 123-08-0/BI
            18 130064-21-0/BI
             9 151533-32-3/BI
            23 151533-34-5/BI
          2032 156-38-7/BI
            52 17720-60-4/BI
          3938 18162-48-6/BI
            49 182167-02-8/BI
            79 182167-03-9/BI
            10 182167-04-0/BI
             3 182167-05-1/BI
             3 182167-06-2/BI
             2 182167-07-3/BI
             2 182167-08-4/BI
             2 182167-09-5/BI
             2 182167-10-8/BI
             2 182167-11-9/BI
             3 182167-12-0/BI
             2 182167-13-1/BI
             2 182167-14-2/BI
             2 182167-15-3/BI
             2 182167-17-5/BI
             2 182167-19-7/BI
             2 182167-21-1/BI
             2 182167-23-3/BI
             2 182167-26-6/BI
             1 182167-28-8/BI
             2 182167-31-3/BI
             2 182167-32-4/BI
             2 182167-34-6/BI
             2 182167-36-8/BI
             2 182167-38-0/BI
             2 182167-39-1/BI
             2 182167-40-4/BI
             2 182167-41-5/BI
             2 182167-43-7/BI
             2 182167-47-1/BI
             9 182167-49-3/BI
             1 182167-53-9/BI
             1 182167-54-0/BI
             1 182167-56-2/BI
             6 182167-58-4/BI
             8 182167-59-5/BI
             2 182330-08-1/BI
           418 1932-03-2/BI
           448 2008-75-5/BI
            43 26815-04-3/BI
          1298 3144-16-9/BI
          4421 3282-30-2/BI
L2       37880 (108-46-3/BI OR 110-87-2/BI OR 123-08-0/BI OR 130064-21-0/BI OR
               151533-32-3/BI OR 151533-34-5/BI OR 156-38-7/BI OR 17720-60-4/BI
                OR 18162-48-6/BI OR 182167-02-8/BI OR 182167-03-9/BI OR 182167-
               04-0/BI OR 182167-05-1/BI OR 182167-06-2/BI OR 182167-07-3/BI
               OR 182167-08-4/BI OR 182167-09-5/BI OR 182167-10-8/BI OR 182167-
               11-9/BI OR 182167-12-0/BI OR 182167-13-1/BI OR 182167-14-2/BI
               OR 182167-15-3/BI OR 182167-17-5/BI OR 182167-19-7/BI OR 182167-
               21-1/BI OR 182167-23-3/BI OR 182167-26-6/BI OR 182167-28-8/BI
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OR 182167-31-3/BI OR 182167-32-4/BI OR 182167-34-6/BI OR 182167-36-8/BI OR 182167-38-0/BI OR 182167-39-1/BI OR 182167-40-4/BI OR 182167-41-5/BI OR 182167-43-7/BI OR 182167-47-1/BI OR 182167-49-3/BI OR 182167-53-9/BI OR 182167-54-0/BI OR 182167-56-2/BI OR 182167-58-4/BI OR 182167-59-5/BI OR 182330-08-1/BI OR 1932-03-2/BI OR 2008-75-5/BI OR 26815-04-3/BI OR 3144-16-9/BI OR 3282-30-2/BI)

=> S 182167-02-8/RN

L3 1 182167-02-8/RN

=> SET NOTICE 1 DISPLAY

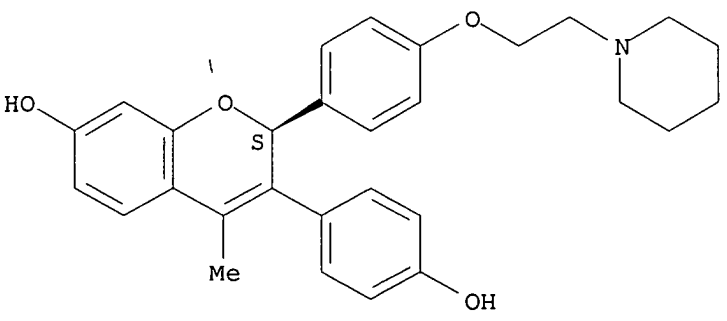
NOTICE SET TO 1 U.S. DOLLAR FOR DISPLAY COMMAND
SET COMMAND COMPLETED

=> D L3 SQIDE 1-

YOU HAVE REQUESTED DATA FROM 1 ANSWERS - CONTINUE? Y/(N):y
THE ESTIMATED COST FOR THIS REQUEST IS 6.15 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN **182167-02-8** REGISTRY
CN 2H-1-Benzopyran-7-ol, 3-(4-hydroxyphenyl)-4-methyl-2-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H-1-Benzopyran-7-ol, 3-(4-hydroxyphenyl)-4-methyl-2-[4-[2-(1-piperidinyl)ethoxy]phenyl]-, (S)-
OTHER NAMES:
CN Acolbifene
CN EM 652
CN Sch 57068
FS STEREOSEARCH
MF C29 H31 N O4
CI COM
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, EMBASE, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
DT.CA CAplus document type: Dissertation; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

49 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
49 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L7 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:816021 CAPLUS
DOCUMENT NUMBER: 132:117704
TITLE: The anti-estrogen hydroxytamoxifen is a potent antagonist in a novel yeast system
AUTHOR(S): Liu, Jia Wei; Jeannin, Elisabeth; Picard, Didier
CORPORATE SOURCE: Dep. Biologie Cellulaire, Univ. Geneve, Geneva, CH-1211, Switz.
SOURCE: Biological Chemistry (1999), 380(11), 1341-1345
CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: Walter de Gruyter GmbH & Co. KG
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:580516 CAPLUS
DOCUMENT NUMBER: 131:306858
TITLE: The interaction of raloxifene and the active metabolite of the antiestrogen EM-800 (SC 5705) with the human estrogen receptor
AUTHOR(S): Schafer, Jennifer I. MacGregor; Liu, Hong; Tonetti, Debra A.; Jordan, V. Craig
CORPORATE SOURCE: Robert H. Lurie Comprehensive Cancer Center, Northwestern University Medical School, Chicago, IL, 60611, USA
SOURCE: Cancer Research (1999), 59(17), 4308-4313
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:437555 CAPLUS
DOCUMENT NUMBER: 131:208327
TITLE: EM-652 (SCH 57068), a third generation SERM acting as pure antiestrogen in the mammary gland and endometrium
AUTHOR(S): Labrie, Fernand; Labrie, Claude; Belanger, Alain; Simard, Jacques; Gauthier, Sylvain; Luu-The, Van; Merand, Yves; Giguere, Vincent; Candas, Bernard; Luo, Shouqi; Martel, Celine; Singh, Shankar Mohan; Fournier, Marc; Coquet, Agnes; Richard, Virgile; Charbonneau, Ronald; Charpenet, Gilles; Tremblay, Andre; Tremblay, Gilles; Cusan, Lionel; Veilleux, Raymonde
CORPORATE SOURCE: Oncology and Molecular Endocrinology Research Center, Centre Hospitalier Universitaire de Quebec (CHUQ), Pavilion CHUL, Department of Medicine, Laval University, Quebec, QC, G1V 4G2, Can.
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (1999), 69(1-6), 51-84
CODEN: JSBBEZ; ISSN: 0960-0760
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 224 THERE ARE 224 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:320183 CAPLUS
DOCUMENT NUMBER: 129:62418
TITLE: Binding characteristics of novel nonsteroidal antiestrogens to the rat uterine estrogen receptors

AUTHOR(S): Martel, Celine; Provencher, Louis; Li, Xun; St. Pierre, Alain; Leblanc, Gilles; Gauthier, Sylvain; Merand, Yves; Labrie, Fernand
CORPORATE SOURCE: Laboratory of Molecular Endocrinology, CHUL Research Center, QC, G1V 4G2, Can.
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (1998), 64(3-4), 199-205
CODEN: JSBBEZ; ISSN: 0960-0760
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:153797 CAPLUS
DOCUMENT NUMBER: 128:266369
TITLE: Ligand-independent activation of the estrogen receptors α and β by mutations of a conserved tyrosine can be abolished by antiestrogens
AUTHOR(S): Tremblay, Gilles B.; Tremblay, Andre; Labrie, Fernand; Giguere, Vincent
CORPORATE SOURCE: Molecular Oncology Group, Royal Victoria Hospital, Montreal, QC, H3A 1A1, Can.
SOURCE: Cancer Research (1998), 58(5), 877-881
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

L7 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:11899 CAPLUS
DOCUMENT NUMBER: 128:149270
TITLE: EM-800, a novel antiestrogen, acts as a pure antagonist of the transcriptional functions of estrogen receptors α and β
AUTHOR(S): Tremblay, Andre; Tremblay, Gilles B.; Labrie, Claude; Labrie, Fernand; Giguere, Vincent
CORPORATE SOURCE: Molecular Oncology Group, Royal Victoria Hospital, Montreal, QC, H3A 1A1, Can.
SOURCE: Endocrinology (1998), 139(1), 111-118
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:693477 CAPLUS
DOCUMENT NUMBER: 128:10399
TITLE: Characterization of the effects of the novel non-steroidal antiestrogen EM-800 on basal and estrogen-induced proliferation of T-47D, ZR-75-1 and MCF-7 human breast cancer cells in vitro
AUTHOR(S): Simard, Jacques; Labrie, Claude; Belanger, Alain; Gauthier, Sylvain; Singh, Shankar M.; Merand, Yves; Labrie, Fernand
CORPORATE SOURCE: Laboratory of Molecular Endocrinology, CHUL Research Center, QC, Can.
SOURCE: International Journal of Cancer (1997), 73(1), 104-112
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:560295 CAPLUS
DOCUMENT NUMBER: 127:242889
TITLE: Blockade of the stimulatory effect of estrogens, OH-tamoxifen, OH-toremifene, droloxifene, and raloxifene on alkaline phosphatase activity by the antiestrogen EM-800 in human endometrial adenocarcinoma Ishikawa cells
AUTHOR(S): Simard, Jacques; Sanchez, Rocio; Poirier, Donald; Gauthier, Sylvain; Singh, Shankar M.; Merand, Yves; Belanger, Alain; Labrie, Claude; Labrie, Fernand
CORPORATE SOURCE: Laboratory of Molecular Endocrinology, CHUL Research Center, Quebec, QC, GIV 4G2, Can.
SOURCE: Cancer Research (1997), 57(16), 3494-3497
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:296289 CAPLUS
DOCUMENT NUMBER: 127:31462
TITLE: Response of symbiotic endomycorrhizal fungi to estrogens and antiestrogens
AUTHOR(S): Poulin, Marie-Josee; Simard, Jacques; Catford, Jean-Guy; Labrie, Fernand; Piche, Yves
CORPORATE SOURCE: Centre de Recherche en Biologie Forestiere, Faculte de Foresterie et de Geomatique, Universite Laval, Sainte-Foy, QC, G1K 7P4, Can.
SOURCE: Molecular Plant-Microbe Interactions (1997), 10(4), 481-487
CODEN: MPMIEL; ISSN: 0894-0282
PUBLISHER: American Phytopathological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

was also found to block the recruitment of SRC-1 at AF1 of ERβ, this ligand-independent activation of AF1 being closely. . . protein kinase. Most importantly, the antiestrogen hydroxytamoxifen has no inhibitory effect on the SRC-1-induced ERβ activity while the pure antiestrogen **EM-652** completely abolishes this effect, thus strengthening the need to use pure antiestrogens in breast cancer therapy in order to control. . . up to 5 yr become neg. at longer time intervals and why resistance develops to tamoxifen. EM-800, the prodrug of **EM-652**, has been shown to prevent the development of dimethylbenz(a)anthracene (DMBA)-induced mammary carcinoma in the rat, a well-recognized model of human. . . Uterine size was reduced to castration levels in the groups of animals treated with EM-800. An almost complete disappearance of **estrogen** receptors was observed in the uterus, vaginum and tumors in nude mice treated with EM-800. **EM-652** was the most potent antiestrogen to inhibit the growth of human breast cancer ZR-75-1, MCF-7 and T-47D cells in vitro when compared with ICI 182780, ICI 164384, hydroxytamoxifen, and droloxifene. Moreover, **EM-652** and EM-800 have no stimulatory effect on the basal levels of cell proliferation in the absence of E2 while hydroxytamoxifen and droloxifene had a stimulatory effect on the basal growth of T-47D and ZR-75-1 cells. **EM-652** was also the most potent inhibitor of the percentage of cycling cancer cells. When human breast cancer ZR-75-1 xenografts were grown in nude mice, EM-800 led to a complete inhibition of the stimulatory effect of **estrogens** in ovariectomized mice while tamoxifen was less potent and even stimulated the growth of the tumors in the absence of **estrogens**, thus illustrating the stimulatory effect of tamoxifen on breast cancer growth. When incubated with human Ishikawa endometrial carcinoma cells, EM-800 had no stimulatory effect on alkaline phosphatase activity, an **estrogen**-sensitive parameter. Raloxifene, droloxifene, hydroxytoremifene and hydroxytamoxifen, on the other hand, all stimulated to various extent, the activity of this enzyme.. . . tamoxifen failure patients where EM-800 (SCH 57050) is compared to Arimidex. The detailed information obtained at the preclin. level with **EM-652** or EM-800 indicates that these orally active compds. are highly potent and pure antiestrogens in the mammary gland and endometrium. . .

IT **Estrogens**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiestrogens; activity of **EM-652** (**SCH 57068**) antiestrogen in mammary gland and endometrium)

IT **Estrogen** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α and β; activity of **EM-652** (**SCH 57068**) antiestrogen in mammary gland and endometrium)

L7 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

AB Tamoxifen (TAM), the only antiestrogen currently available for the endocrine therapy of breast cancer behaves as a mixed agonist/antagonist of **estrogen** action, thus limiting its therapeutic potential. We report the binding characteristics of a novel series of nonsteroidal antiestrogens to the rat uterine **estrogen** receptor. As measured by competition studies, the affinity of **EM-652**, the active metabolite of the prodrug EM-800, for the **estrogen** receptor is 7-11 times higher than that of 17β- **estradiol** (E2), ICI 182780, and hydroxy-tamoxifen (OH-TAM), the active metabolite of Tamoxifen. **EM-652** is 20+ more potent than ICI 164384 and Droloxifene while it is 400 times more potent than Toremifene in displacing [3H]E2 from the rat uterine **estrogen** receptor. On the other hand, the prodrug EM-800 and Tamoxifen have resp. 150-fold and 410-fold less affinity for the **estrogen** receptor than the pure antiestrogen **EM-652**. No significant binding of **EM-652**, EM-800, TAM or OH-TAM was observed to the rat uterine progesterone receptor at concns. up to 10 000 nM except for TAM that caused a 50% displacement of labeled R5020 at 4000 nM. No

significant binding of **EM-652** or EM-800 was observed on the rat ventral prostate androgen receptor or the rat uterine progesterone receptor. The present data demonstrate the high affinity and specificity of the new antiestrogen, **EM-652**, for the rat uterine **estrogen** receptor. The antiestrogen **EM-652** thus becomes the compound having the highest known affinity for the **estrogen** receptor. Due to its unique potency and its pure antiestrogenic activity already demonstrated in many systems, this antiestrogen could well offer an important advance for the endocrine therapy of breast cancer, uterine cancer, and other **estrogen**-sensitive diseases in women.

IT 50-28-2, 17β-Estradiol, biological studies 10540-29-1, Tamoxifen 68047-06-3, Hydroxy-tamoxifen 82413-20-5, Droloxifene 89778-26-7, Toremifene 98007-99-9, ICI 164384 129453-61-8, ICI 182780 151533-34-5, EM 343 **182167-02-8**, **EM 652** 182167-03-9, EM 800 182167-04-0, EM 762 182167-49-3, EM 776 182167-58-4, EM 651
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding characteristics of nonsteroidal antiestrogens to uterine **estrogen** receptors)

L7 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

AB It has recently been suggested that mutation of a conserved tyrosine to asparagine within the ligand-binding domain of the **estrogen** receptor (ER) α confers hormone-independent activation and insensitivity to antiestrogens. In view of the recent discovery of ERβ and the development of the novel nonsteroidal antiestrogen EM-800 and its active metabolite **EM-652**, the authors decided to reexamine this issue by introducing a series of mutations at the conserved tyrosine 537 in ERα and 443 in ERβ and measuring their transcriptional activity in the absence and presence of **estradiol** and the antiestrogens **EM-652**, ICI 182,780, and 4-hydroxytamoxifen. As demonstrated previously for ERα, the authors observed that substituting a serine or asparagine but not. . .

IT 68047-06-3, 4-Hydroxytamoxifen 129453-61-8, ICI-182780 **182167-02-8**, **EM 652**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ligand-independent activation of the **estrogen** receptors α and β by mutations of a conserved tyrosine can be abolished by antiestrogens)

L7 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

AB **Estrogens** act as potent mitogens in a large number of breast cancers, and the use of **estrogen** receptor (ER) antagonists is, therefore, considered the endocrine therapy of choice in the management of this disease. We describe the mol. properties of **EM-652**, the active metabolite of EM-800, a novel nonsteroidal antiestrogen compound, on the transcriptional functions of ERα and ERβ. Using RT-PCR, . . . that both receptors should be considered putative targets for antiestrogen action in the breast. In cotransfection assays using a synthetic **estrogen**-responsive promoter, **EM-652** shows no agonistic activity on ERα and ERβ transcriptional function and blocks the **estradiol** (E2)-mediated activation of both ERα and ERβ. **EM-652** is also very effective in abrogating E2-stimulated ERα and ERβ trans-activation of the pS2 promoter in HeLa cells. **EM-652** does not alter binding of ERα and ERβ to DNA. The Ras-mediated induction of ERα and ERβ transcriptional activity in the presence of E2 is also completely abolished by **EM-652**. In addition, **EM-652** blocks the E2-dependent activation of ERα and ERβ by the steroid hormone receptor coactivator-1 as well as the in vitro. . .

IT **182167-02-8**, **EM 652** 182167-03-9, EM-800
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EM-800, a novel antiestrogen, acts as a pure antagonist of the transcriptional functions of **estrogen** receptors α and β)

L7 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
AB Since **estrogens** play a predominant role in the development and growth of human breast cancer, antiestrogens represent a logical approach to the treatment of this disease. The present study compares the effects of the novel non-steroidal anti-**estrogen** EM-800 and related compds. with those of a series of anti-**estrogens** on basal and 17β- **estradiol** (E2)-induced cell proliferation in human breast cancer cell lines. In the absence of added E2, EM-800 and related compds. failed. . . . lines. The stimulation of T-47D cell proliferation induced by 0.1 nM E2 was competitively blocked by a simultaneous incubation with **EM-652**, EM-800, OH-tamoxifen, OH-toremifene, ICI 182780, ICI 164384, droloxifene, tamoxifen and toremifene at apparent Ki values of 0.015, 0.011-0.017, 0.040-0.054, 0.043,. . . and 0.735 nM, approx., 10 nM and >10 nM, resp. Similar data were obtained in ZR-75-1 and/or MCF-7 cells. Moreover, **EM-652** was 6-fold more potent than OH-Tamoxifen in inhibiting the proportion of cycling MCF-7 cells. Our data show that EM-800 and **EM-652** are the most potent known antiestrogens in human breast cancer cells in vitro and that they are devoid of the estrogenic activity of OH-tamoxifen and droloxifene suggested by stimulation of cell growth in the absence of **estrogens** in ZR-75-1 and MCF-7 cells.
IT 10540-29-1, Tamoxifen 68047-06-3, 4-Hydroxy-tamoxifen 82413-20-5, Droloxifene 89778-26-7, Toremifene 98007-99-9, ICI 164384 110503-62-3, 4-Hydroxy toremifene 129453-61-8, ICI 182780 151533-34-5, EM 343 **182167-02-8**, **EM 652** 182167-04-0, EM 762 182167-58-4, EM 651
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of effects of novel non-steroidal antiestrogens on basal and **estrogen**-induced proliferation of T-47D, ZR-75-1 and MCF-7 human breast cancer cells in vitro)

L7 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
AB . . . effects of the novel nonsteroidal pure antiestrogen EM-800 and related compds. with those of a series of antiestrogens on the **estrogen**-sensitive alkaline phosphatase (AP) activity in human endometrial adenocarcinoma Ishikawa cells. Exposure to increasing concns. of up to 1000 nM EM-800 or its active metabolite **EM-652** alone failed to affect basal AP activity. In contrast, incubation with 10 nM (Z)-4-OH-tamoxifen, (Z)-4-OH-toremifene, droloxifene, or raloxifene increased the value of this **estrogen**-sensitive parameter by 3.3-, 3.5-, 2.2-, and 1.6-fold, resp., a stimulatory effect that was completely reversed by simultaneous exposure to 30 nM EM-800. Moreover, the stimulation of AP activity induced by 1 nM 17β- **estradiol** was completely reversed by EM-800, **EM-652**, or ICI-182780, at the IC50 value of 1.98, 1.01, and 5.64 nM, resp., whereas the partial blockade exerted by (Z)-4-OH-tamoxifen,. . . 41.0, and 3.74 nM, resp. Thus, as assessed by their activity in the human Ishikawa endometrial carcinoma cells, EM-800 and **EM-652** are the most potent known antiestrogens in Ishikawa cells, and, most importantly, they are devoid of the estrogenic activity observed. . .
ST antiestrogen **estrogen** alk phosphatase endometrium adenocarcinoma; tamoxifen alk phosphatase endometrium adenocarcinoma; toremifene alk phosphatase endometrium adenocarcinoma; droloxifene alk phosphatase endometrium adenocarcinoma; rodroloxifene alk phosphatase endometrium adenocarcinoma; EM 800 alk phosphatase endometrium adenocarcinoma; **EM 652** alk phosphatase endometrium adenocarcinoma
IT 68047-06-3, Hydroxytamoxifen 82413-20-5, Droloxifene 84449-90-1, Raloxifene 110503-62-3 129453-61-8, ICI-182780 **182167-02-8**, **EM 652** 182167-03-9

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blockade of stimulatory effect of **estrogens**, hydroxytamoxifen, hydroxytoremifene, droloxifene, and raloxifene on alkaline phosphatase activity by the antiestrogen EM-800 in human endometrial adenocarcinoma Ishikawa cells)

L7 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

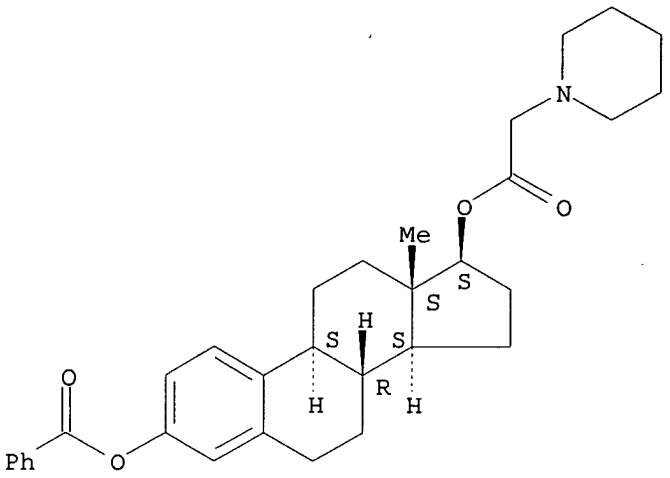
AB Plant flavonoids reported previously to act as mol. signals in the arbuscular mycorrhizal (AM) symbiosis are known to bind to **estrogen** receptors and to exert estrogenic effects on mammalian cells. To further investigate the **estrogen**-like properties of flavonoids the present study examined whether **estrogen** and antiestrogens have flavonoid-related functions in AM fungi. Bioassays were performed in a monoaxenic system with the AM fungi Gigaspora. . . concns. ranging from 0.01 to 10.0 μM shows an estimated EC50 value of 3.26 μM. The present results show that 17β- **estradiol** (III) and II exert similar stimulatory effects in G. intraradices. The agonist effect of II was efficiently suppressed by the new antiestrogen **EM -652** (IV), which is also consistent with the possible presence of **estrogen**-binding sites in AM fungi.

IT 68047-06-3, Hydroxy-tamoxifen 131811-54-6, EM-139 **182167-02-8**, **EM 652**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antiestrogen; response of symbiotic endomycorrhizal fungi to **estrogens** and antiestrogens)

=> d rn str cn 1-5

L1 ANSWER 1 OF 1265 REGISTRY COPYRIGHT 2005 ACS on STN
RN 803618-65-7 REGISTRY

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN **Estradiol, 3-benzoate 1-piperidineacetate (8CI)** (CA INDEX NAME)

L1 ANSWER 2 OF 1265 REGISTRY COPYRIGHT 2005 ACS on STN
RN 786733-95-7 REGISTRY

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

RELATED SEQUENCES AVAILABLE WITH SEQLINK
CN **Protein E2IG5 (human clone DE10316701-SEQID-611 estradiol-induced) (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN 231: PN: DE10316701 PAGE: 1255 claimed sequence

L1 ANSWER 3 OF 1265 REGISTRY COPYRIGHT 2005 ACS on STN
RN 786732-09-0 REGISTRY

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
CN **DNA (human clone DE10316701-SEQID-122 clone E2IG5 estradiol-induced protein cDNA plus flanks) (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN 50: PN: DE10316701 PAGE: 874 claimed DNA

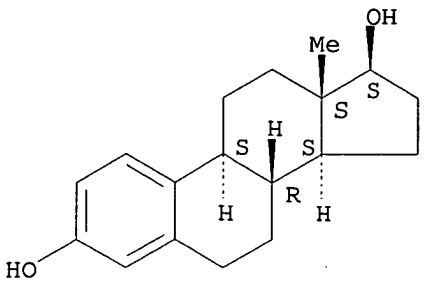
L1 ANSWER 4 OF 1265 REGISTRY COPYRIGHT 2005 ACS on STN
RN 736967-60-5 REGISTRY
CN Estra-1,3,5(10)-triene-3,17-diol (17β)-, compd. with methanol (2:1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Estradiol compd. with methanol (2:1)**

CM 1

H_3C-OH

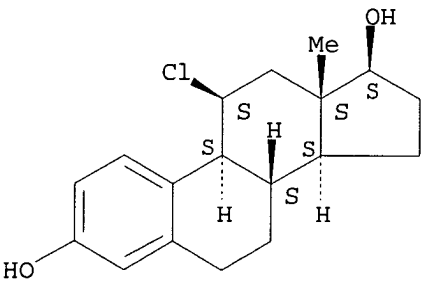
CM 2

Absolute stereochemistry.



L1 ANSWER 5 OF 1265 REGISTRY COPYRIGHT 2005 ACS on STN
RN 668276-95-7 REGISTRY

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Estra-1,3,5(10)-triene-3,17-diol, 11-chloro-, (11β,17β)- (9CI)
(CA INDEX NAME)
OTHER NAMES:
CN **11β-Chloroestradiol**

```
=> e labrie f/in
E1          12     LABRIE CRAIG B/IN
E2           2     LABRIE DAVID WILLIAM/IN
E3           0 --> LABRIE F/IN
E4          86     LABRIE FERNAND/IN
E5           1     LABRIE JACQUES/IN
E6           2     LABRIE JACQUES J/IN
E7           2     LABRIE JACQUES JOSEPH/IN
E8           1     LABRIE JAMES J/IN
E9           1     LABRIE JAMES R/IN
E10          3     LABRIE JEAN PIERRE/IN
E11          2     LABRIE KIMBERLY D/IN
E12          1     LABRIE MARCEL/IN

=> s e4 and l10
L11          9 "LABRIE FERNAND"/IN AND L10

=> d ibib 1-9

L11  ANSWER 1 OF 9  USPATFULL on STN
ACCESSION NUMBER:        2004:203920  USPATFULL
TITLE:                   Medical uses of a selective estrogen receptor modulator
                         in combination with sex steroid precursors
INVENTOR(S):             Labrie, Fernand, Sainte-foy, CANADA
PATENT ASSIGNEE(S):      Endorecherche, Inc. (U.S. individual)

                              NUMBER         KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2004157812      A1   20040812
APPLICATION INFO.:       US 2003-749981     A1   20031230  (10)
RELATED APPLN. INFO.:    Division of Ser. No. US 1999-330799, filed on 11 Jun
                         1999, GRANTED, Pat. No. US 6670346 Continuation-in-part
                         of Ser. No. US 1998-96284, filed on 11 Jun 1998,
                         GRANTED, Pat. No. US 6465445
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    OSTROLENK FABER GERB & SOFFEN, 1180 AVENUE OF THE
                         AMERICAS, NEW YORK, NY, 100368403
NUMBER OF CLAIMS:        34
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      17 Drawing Page(s)
LINE COUNT:              2192
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11  ANSWER 2 OF 9  USPATFULL on STN
ACCESSION NUMBER:        2004:72633  USPATFULL
TITLE:                   Methods of treating and/or suppressing weight gain
INVENTOR(S):             Labrie, Fernand, Quebec, CANADA
                         Deshaies, Yves, Quebec, CANADA
                         Richard, Denis, Quebec, CANADA
                         Martel, Celine, Quebec, CANADA
                         Marette, Andre, Quebec, CANADA
PATENT ASSIGNEE(S):      Endorecherche, Inc., CANADA (non-U.S. corporation)

                              NUMBER         KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 6710059         B1   20040323
APPLICATION INFO.:       US 2000-610286          20000706  (9)

                              NUMBER         DATE
                         ---------------- --------
PRIORITY INFORMATION:    US 1999-142407P    19990706 (60)
DOCUMENT TYPE:           Utility
FILE SEGMENT:            GRANTED
PRIMARY EXAMINER:        Seaman, D. Margaret
LEGAL REPRESENTATIVE:    Ostrolenk, Faber, Gerb & Soffen LLP
NUMBER OF CLAIMS:        33
EXEMPLARY CLAIM:         1
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NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 2266
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 3 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2004:45007 USPATFULL
TITLE: Methods of treating and/or suppressing insulin resistance
INVENTOR(S): **Labrie, Fernand**, Quebec, CANADA
Deshaies, Yves, Quebec, CANADA
Richard, Denis, Quebec, CANADA
Martel, Celine, Quebec, CANADA
Marette, Andre, Quebec, CANADA
PATENT ASSIGNEE(S): Endorecherche, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004034000	A1	20040219
APPLICATION INFO.:	US 2003-387043	A1	20030310 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-610286, filed on 6 Jul 2000, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-142407P	19990706 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: OSTROLENK, FABER, GERB & SOFFEN, LLP, 1180 Avenue of the Americas, New York, NY, 10036-8403
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 2230
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 4 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2003:337283 USPATFULL
TITLE: Medical uses of a selective estrogen receptor modulator in combination with sex steroid precursors
INVENTOR(S): **Labrie, Fernand**, Sainte-foy, CANADA
PATENT ASSIGNEE(S): Endorecherche, Inc., CANADA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6670346	B1	20031230
APPLICATION INFO.:	US 1999-330799		19990611 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-96284, filed on 11 Jun 1998, now patented, Pat. No. US 6465445
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Criares, Theodore J.
ASSISTANT EXAMINER: Kim, Jennifer
LEGAL REPRESENTATIVE: Ostrolenk, Faber, Gerb & Soffen, LLP
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Figure(s); 17 Drawing Page(s)
LINE COUNT: 2384
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 5 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2003:93647 USPATFULL
TITLE: Selective estrogen receptor modulators in combination with estrogens
INVENTOR(S): **Labrie, Fernand**, Sainte-foy, CANADA
PATENT ASSIGNEE(S): Endorecherche, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE

PATENT INFORMATION: US 2003065008 A1 20030403
APPLICATION INFO.: US 2002-143894 A1 20020509 (10)
RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-771180, filed on 26 Jan 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-178601P	20000128 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: OSTROLENK FABER GERB & SOFFEN, 1180 AVENUE OF THE AMERICAS, NEW YORK, NY, 100368403
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 3036
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 6 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2003:57944 USPATFULL
TITLE: Selective estrogen receptor modulators in combination with estrogens
INVENTOR(S): **Labrie, Fernand**, Sainte-foy, CANADA
PATENT ASSIGNEE(S): Endorecherche, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003040510	A1	20030227
APPLICATION INFO.:	US 2001-52824	A1	20011107 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-771180, filed on 26 Jan 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-178601P	20000128 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: OSTROLENK FABER GERB & SOFFEN, 1180 AVENUE OF THE AMERICAS, NEW YORK, NY, 100368403
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 2854
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 7 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2002:344449 USPATFULL
TITLE: Selective estrogen receptor modulators in combination with estrogens
INVENTOR(S): **Labrie, Fernand**, Sainte-foy, CANADA
PATENT ASSIGNEE(S): Endorecherche, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002198179	A1	20021226
APPLICATION INFO.:	US 2001-52803	A1	20011107 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-771180, filed on 26 Jan 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-178601P	20000128 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: OSTROLENK FABER GERB & SOFFEN, 1180 AVENUE OF THE AMERICAS, NEW YORK, NY, 100368403
NUMBER OF CLAIMS: 43
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 3044
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 8 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2002:268744 USPATFULL
TITLE: Medical uses of a selective estrogen receptor modulator in combination with sex steroid precursors
INVENTOR(S): **Labrie, Fernand**, Sainte-foy, CANADA
PATENT ASSIGNEE(S): Endorecherche, Inc., CANADA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6465445	B1	20021015
APPLICATION INFO.:	US 1998-96284		19980611 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Criares, Theodore J.
ASSISTANT EXAMINER: Kim, Jennifer
LEGAL REPRESENTATIVE: Ostrolenk, Faber, Gerb & Soffen LLP
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Figure(s); 13 Drawing Page(s)
LINE COUNT: 2377
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 9 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2000:57797 USPATFULL
TITLE: Benzopyran-containing compounds and method for their use
INVENTOR(S): **Labrie, Fernand**, Quebec, Canada
Merand, Yves, Quebec, Canada
Gauthier, Sylvain, Quebec, Canada
PATENT ASSIGNEE(S): Endorecherche, Inc., Quebec, Canada (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6060503		20000509
APPLICATION INFO.:	US 1995-388207		19950221 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-285354, filed on 3 Aug 1994, now patented, Pat. No. US 5840735 which is a division of Ser. No. US 1991-801704, filed on 2 Dec 1991, now patented, Pat. No. US 5395842
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Criares, Theodore J.
LEGAL REPRESENTATIVE: Ostrolenk, Faber, Gerb & Soffen, LLP
NUMBER OF CLAIMS: 84
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 1590
CAS INDEXING IS AVAILABLE FOR THIS PATENT.